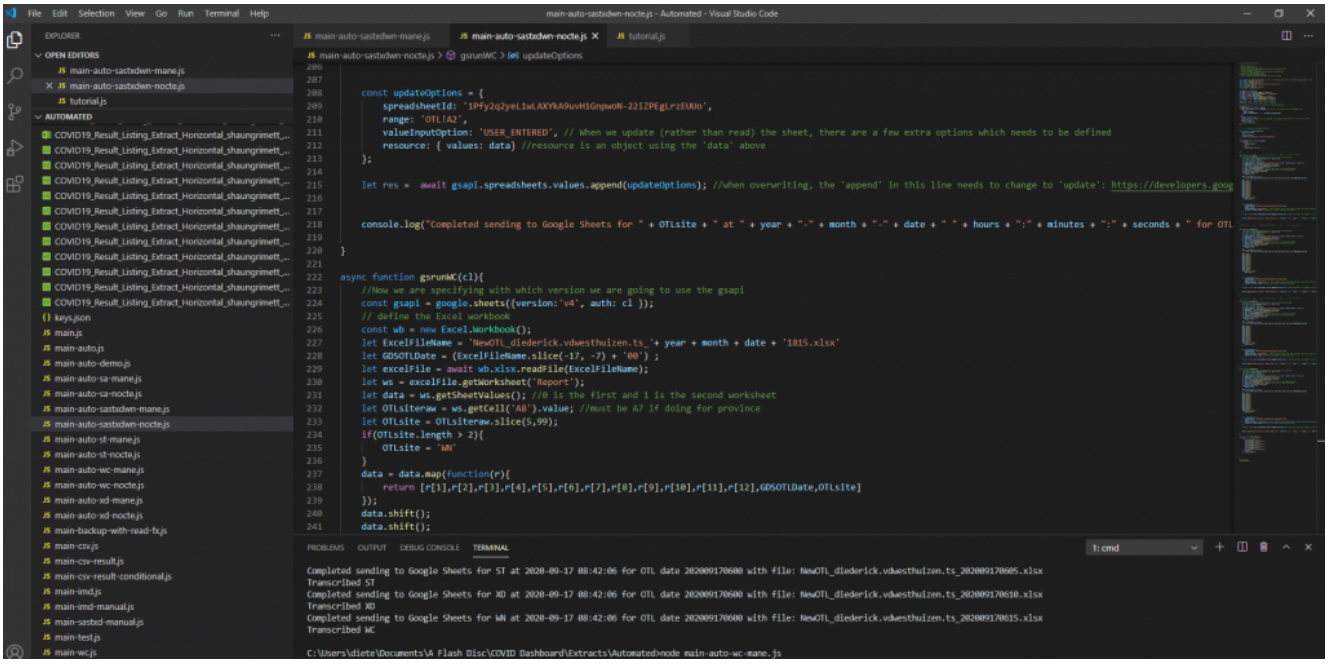
Section 7.8 – COVID OTL Dashboard

A dashboard was created to visually represent the COVID outstanding test list for our province for COVID outstanding PCR tests. This dashboard has been requested by the area manager of the Western Cape and various others on the Virology Expert Committee. Even though not a task primarily assigned to chemical pathologists, since I have an interest in data science, I tried to help. The end result was a dashboard which is updated every morning at 06h00 and every evening at 18h00 with a few JavaScript scripts running each day, updating three databases on the backend along with automated data extractions being done from TrakCare every morning and evening at a predefined time.



Screenshot 1 – Illustration of the JavaScript code to read the extracted Excel (or CSV) files and transcribing them to a Google Sheets database.

This dashboard was used (and likely still are being used) especially by the virologists at Groote Schuur Hospital to track the progress of outstanding COVID PCR tests and it can also be used to show possible bottlenecks in pre-analytical

sample issues if tests are already registered before being sent to any of our laboratories in the Western Cape.

The dashboard consists of a few pages:

https://datastudio.google.com/embed/reporting/aeafe888-d10f-4959-b1f3-928556abd6f6/page/LMPXB

Figure 1 – Screenshot of the Dashboard. Follow the link above to view.

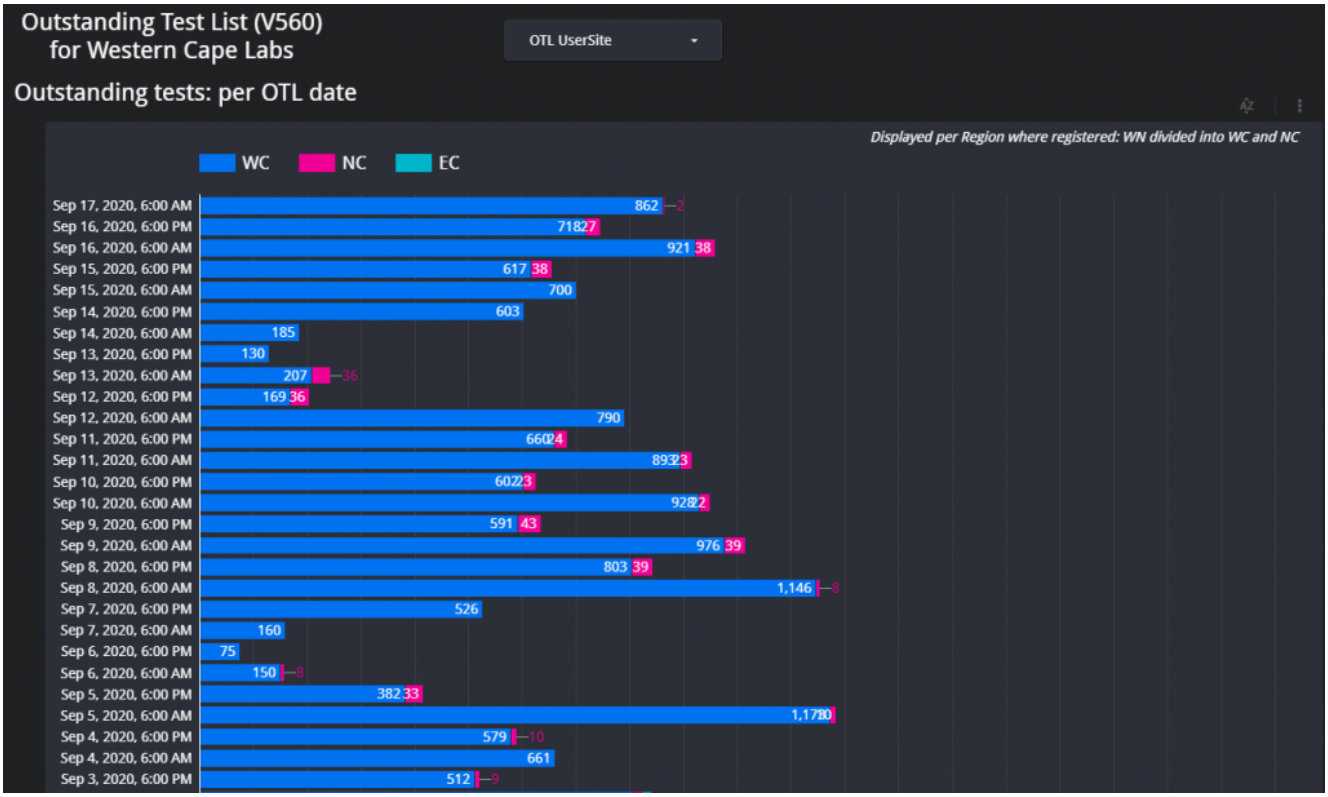


Figure 2 – Example of the layout of the page which shows the total count of items on the respective outstanding test lists for each respective data for the Western Cape.

Figure 3 – Outstanding tests summary by location. This page is especially helpful if the delay / outstanding tests from a specific hospital or clinic needs to be visualized in comparison with other locations (hospitals / clinics).

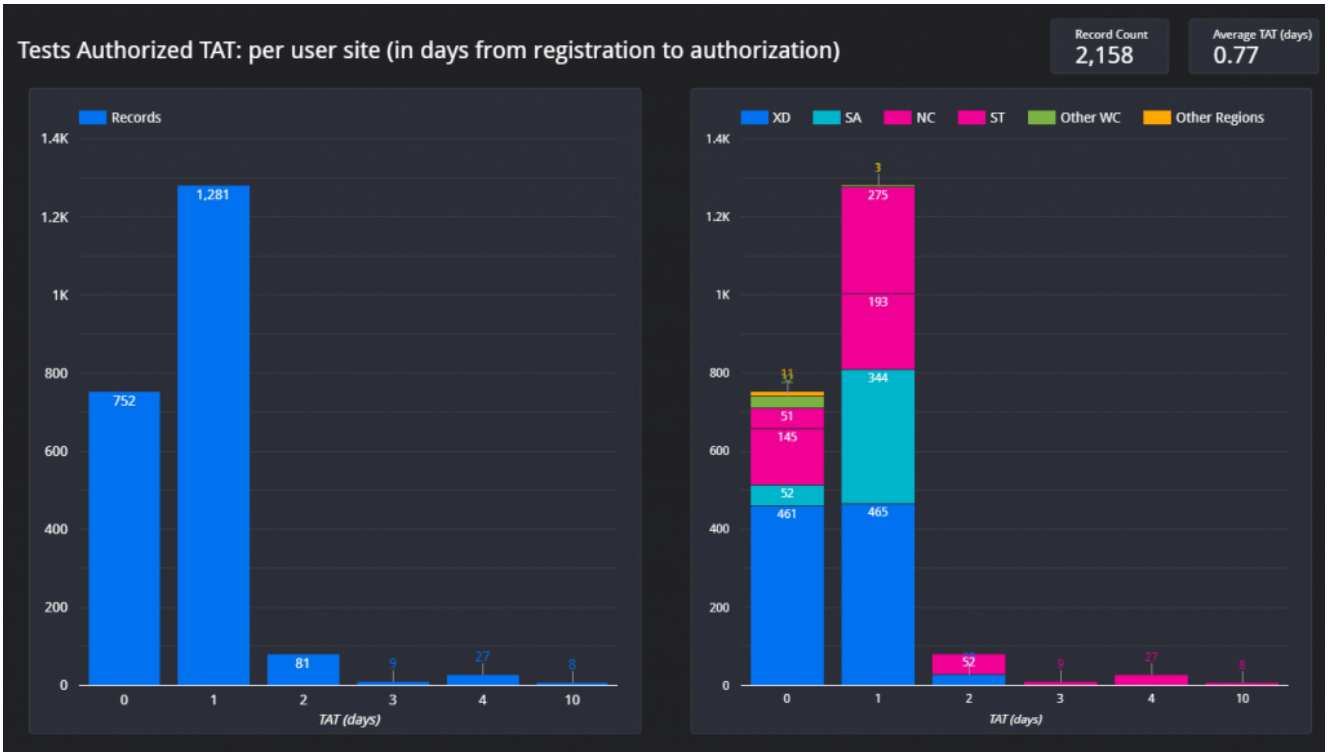


Figure 4 – Illustration of the turnaround time met by a certain count of samples per each respective user site for one day.

Immune Responses to SARS-CoV-2 cause severe COVID-19 in some and recovery in most

Clive Gray – Professor in Immunology
immunopaedia.org – useful web site for immunology resources.

Outline:

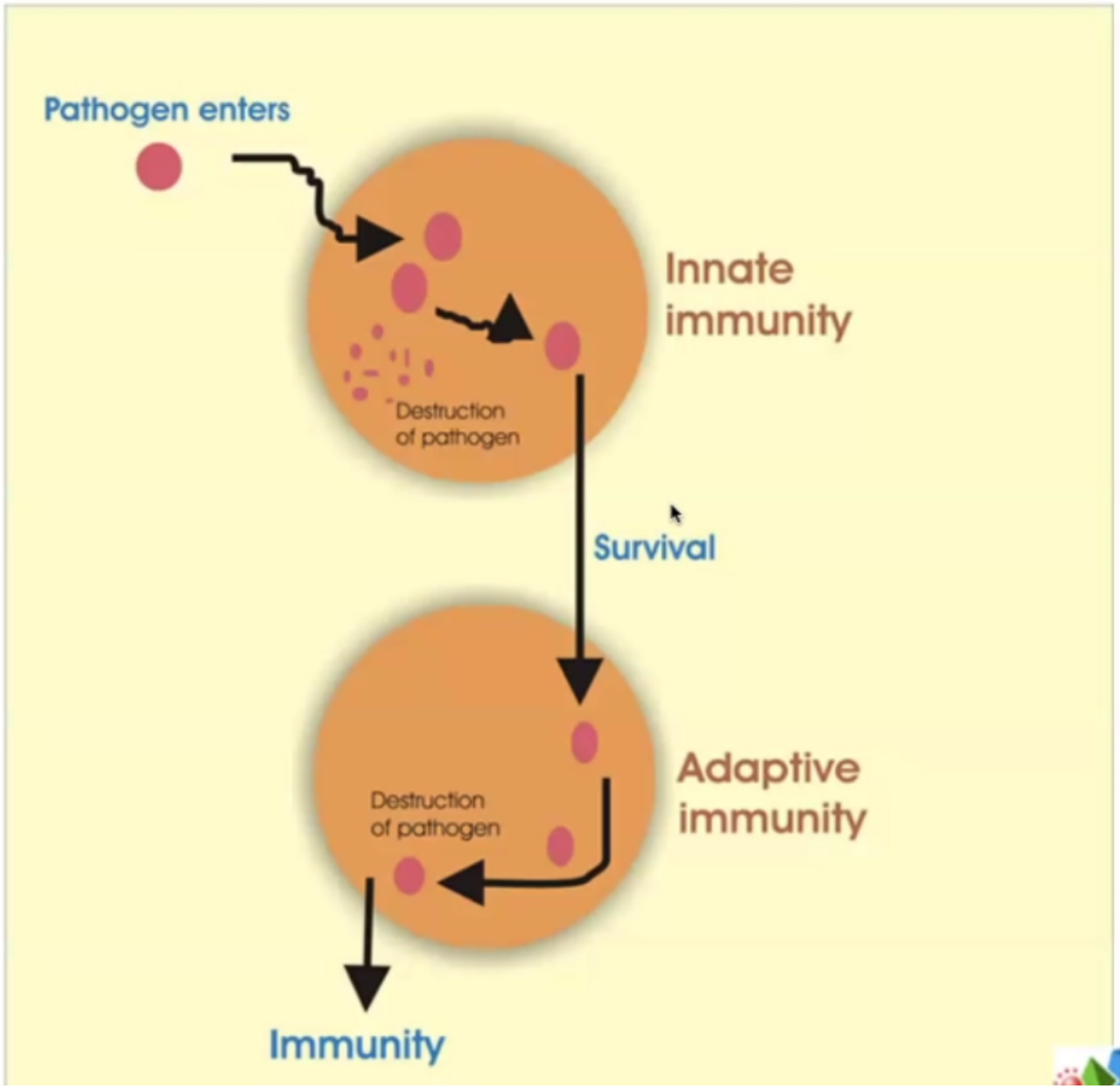
- Basics of Immunology
- A balance between inflammation and tolerance
- What happens to people who progress to severe COVID-19?
- What might be happening in SARS-CoV-2 infected people who remain asymtomatic, have few symptoms and recover?

Internal : External world

~99% of time the pathogen gets destructed, but the pathogen may survive in rare cases.

2 arms of immune responses:

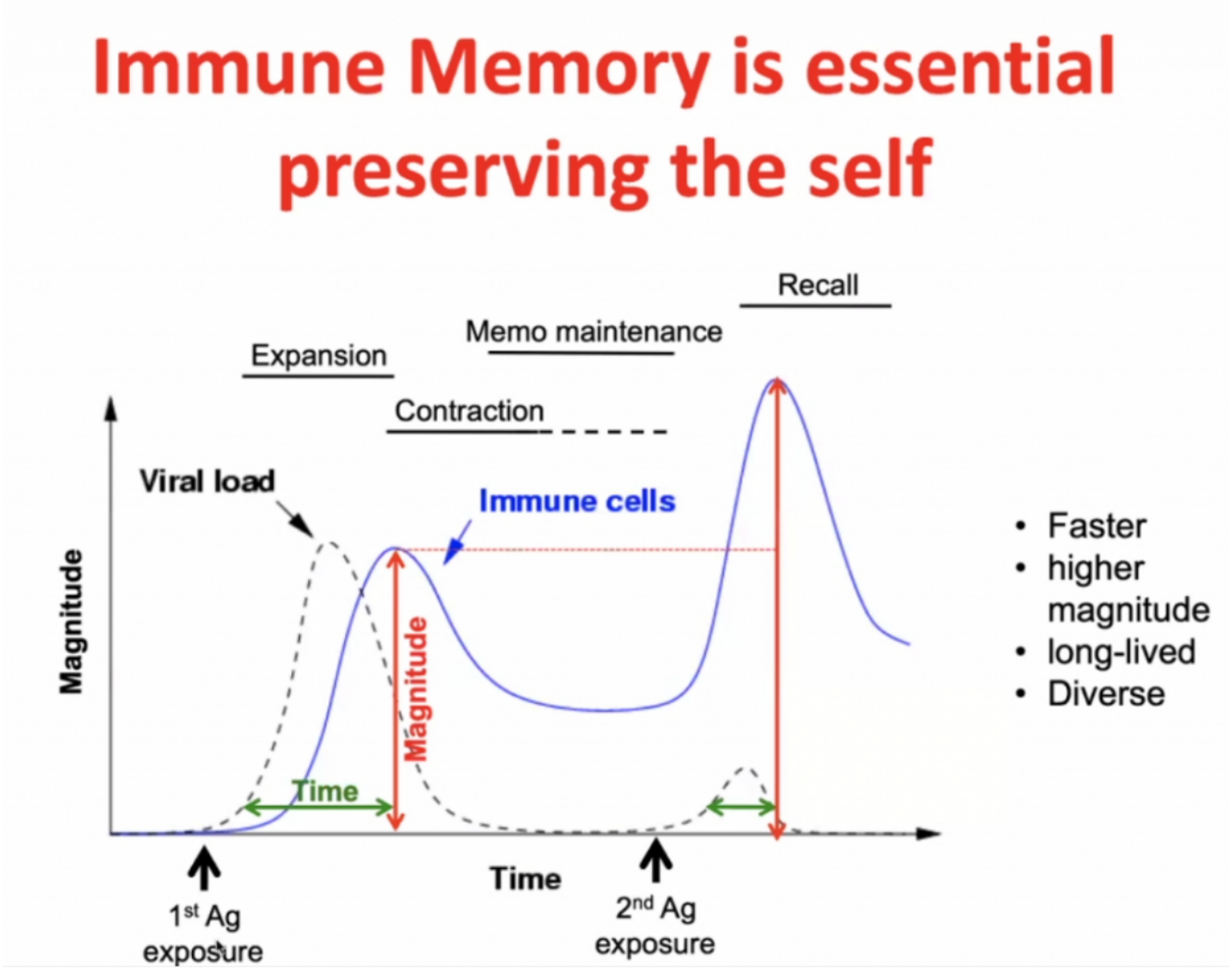
Innate:Acquired Immunity



Innate – evolutionary response – very rapid – elements of innate immunity are found in bacteria, plants, lower vertebrates, squids, fish etc.

Some pathogens survive ->

Adaptive immunity – much more targeted / focussed. The immune system targets more specifically the pathogens which survive the innate immunity.

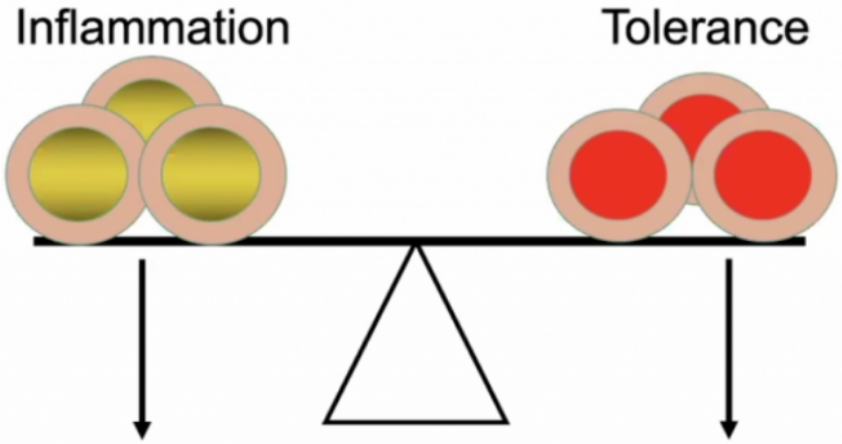


Infection initially -> expansion (peak after maximal viral load) -> contraction with some residual immunity (Memo Maintenance) -> with secondary response (Recall) there is a more rapid expansion (and higher peak) of the specific immunity.

Immune regulation:

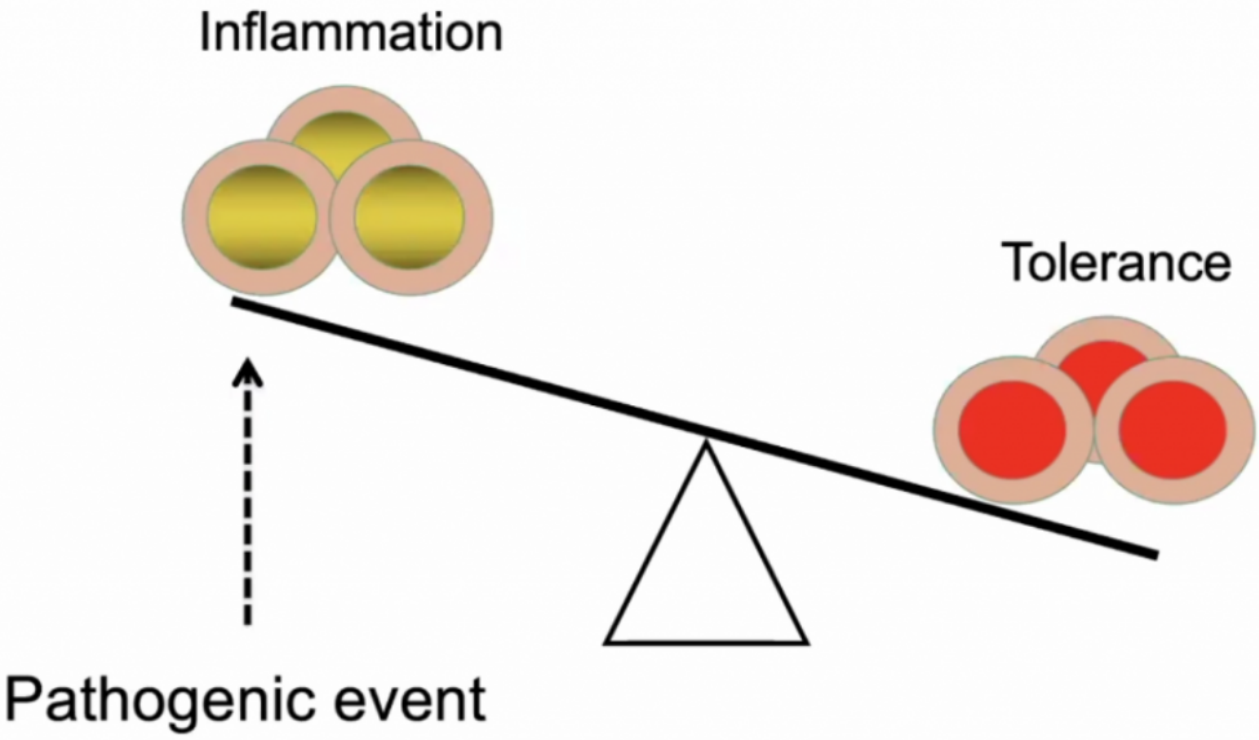
Predisposed conditions: DM, HPT, Obesity, would make an individual highly susceptible to inflammation due to in imbalance of Inflammation vs. Tolerance, see below.

The immunological equilibrium: balance between inflammation and tolerance

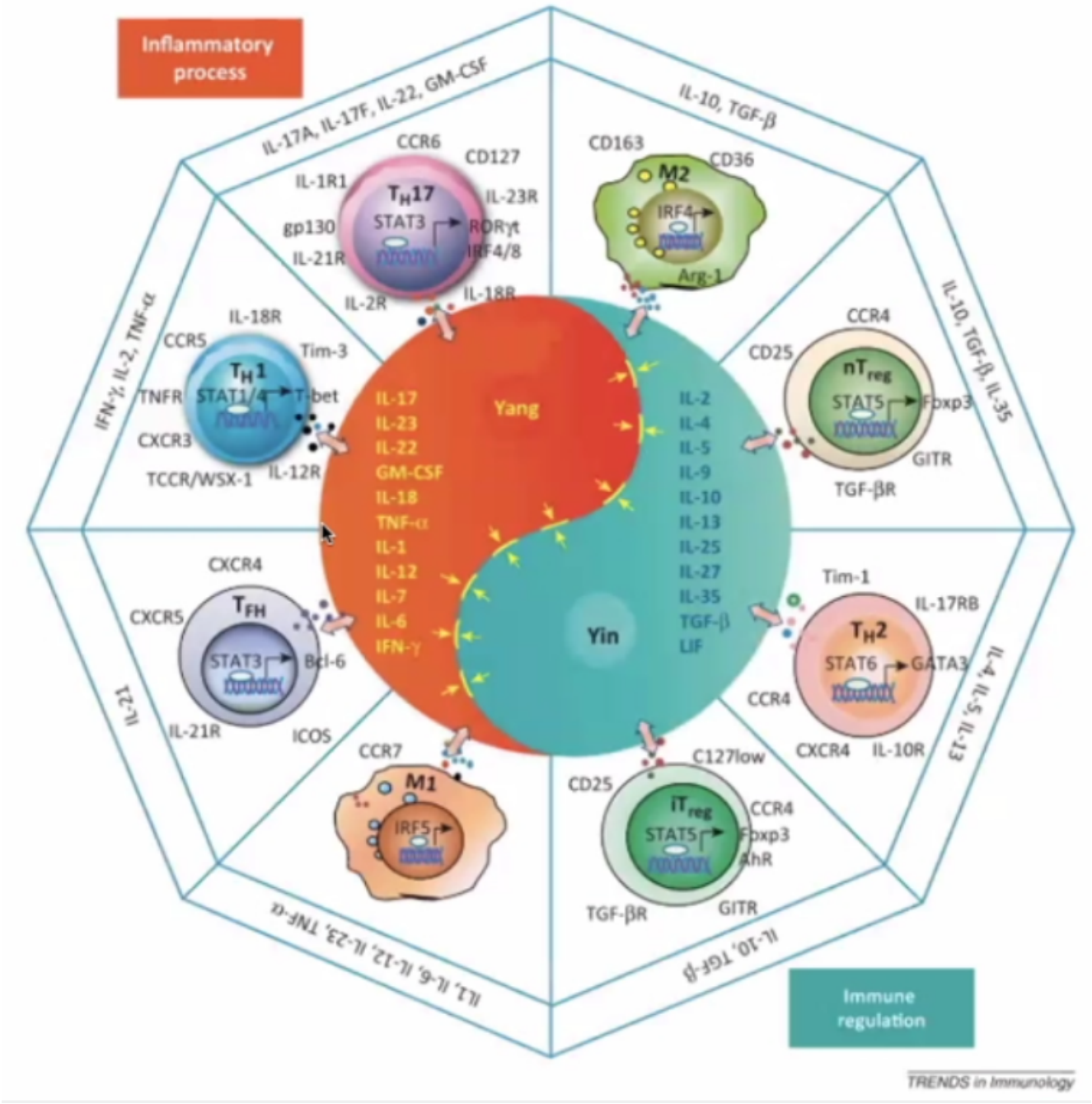


Normal: reactions against pathogens
Pathologic: inflammatory disease, e.g. caused by reactions against self

No response to self
Controlled response to pathogens



The Yin Yang of immunology:



Yin – immune regulation; Yang – Inflammatory Process

Pro-inflammatory (Orange)

TH17 – inflammatory cells secreting the “calling signals” for leucocytes.

TH1 – secreting IFN gamma; IL-2 ; TNF-alpha – cytokines causing inflammation

Macrophage – presents antigens – in lymph nodes and germinal

centres

T-Helper cells T-FH

Immune Regulation (Blue)

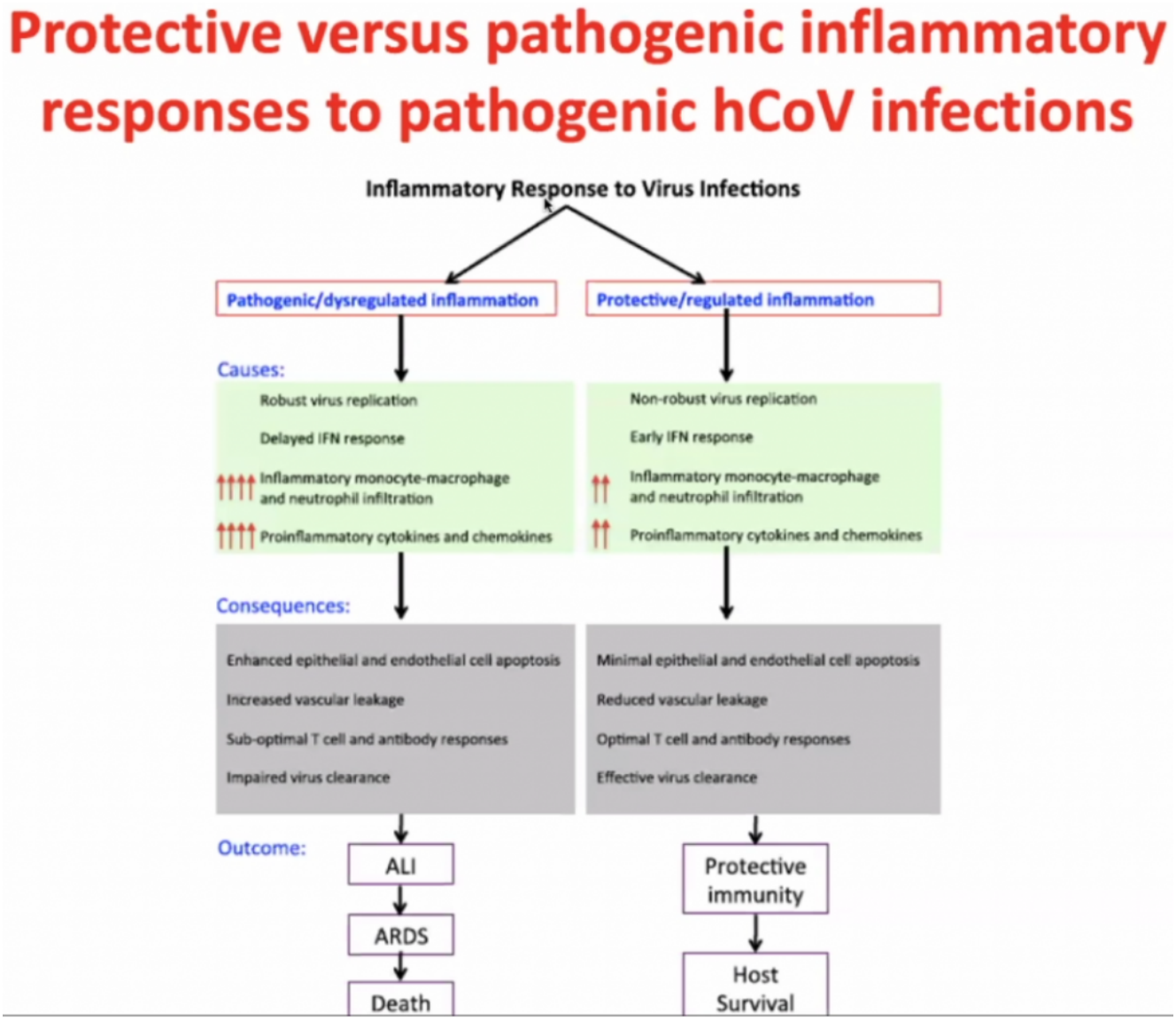
TH2 – hand in hand with TH1 (opposite)

Regulatory cells (nT and iT regulatory cells)

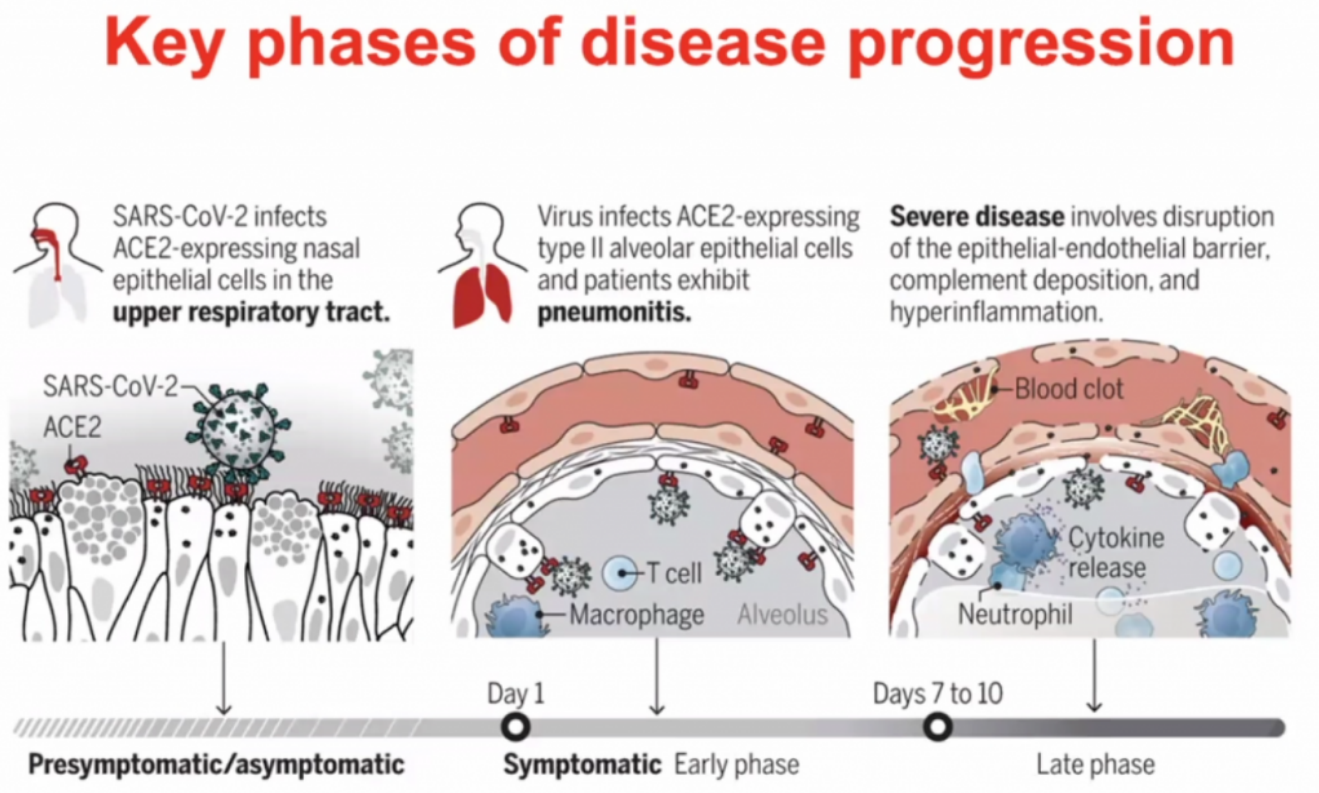
Actual pathogen is not causing disease – but the immune response – thus this is what should be focussed on to treat the disease.

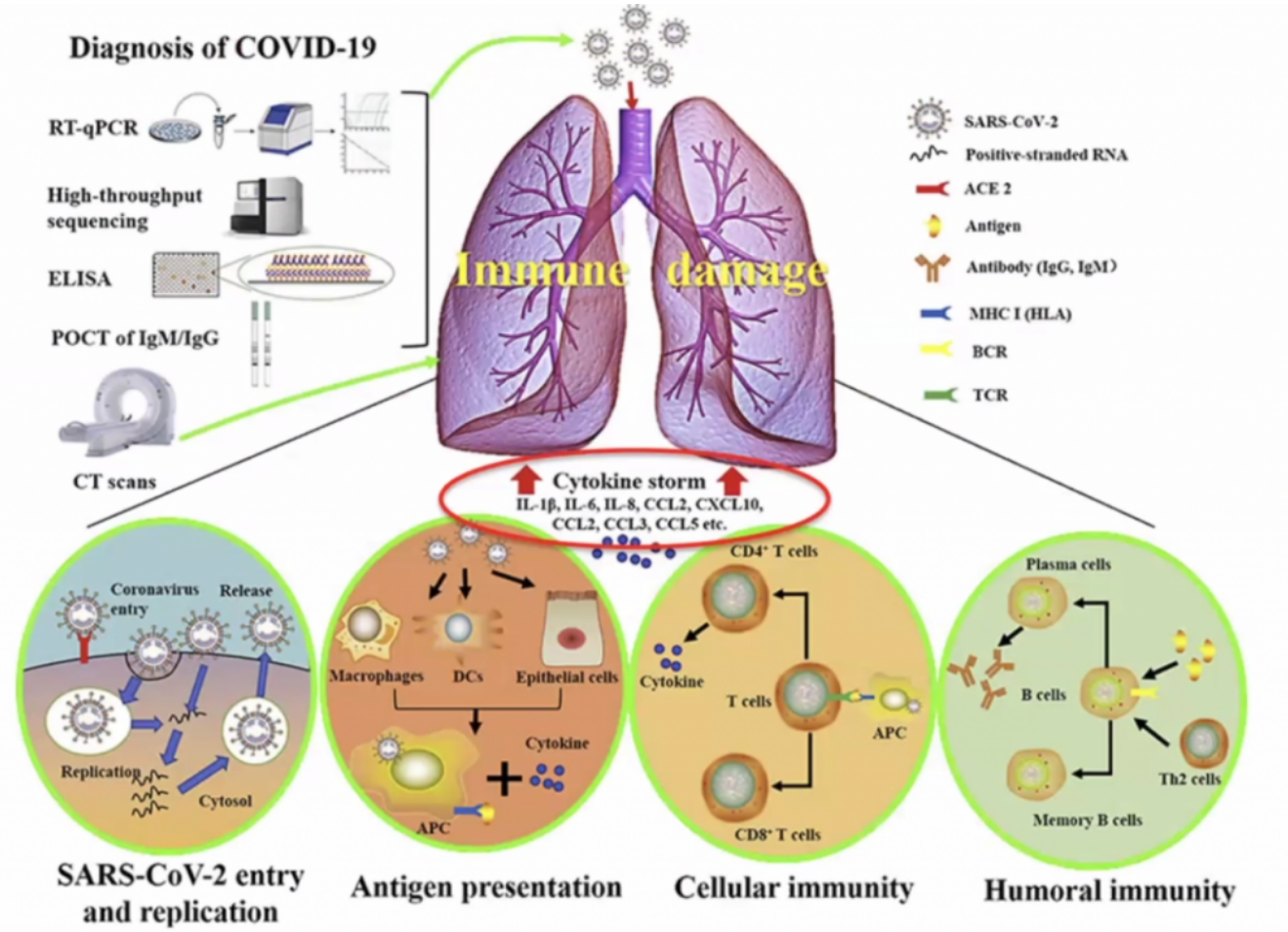
Respiratory Infections

Virus	Entry receptor	Common symptoms	Clinical complications
Rhinovirus	ICAM-1 or LDL	Rhinorrhea, coryza, sneezing, sore throat, cough	Asymptomatic, mild to moderate upper-respiratory tract illness, bronchitis
Common coronavirus	Strain specific	Fever, rhinorrhea, coryza, sneezing, sore throat, cough	Mild to moderate upper-respiratory tract illness
Adenovirus	Strain specific penton	Fever, rhinorrhea, coryza, sneezing, sore throat, cough, pink eye, diarrhea, bladder infections	Mild to moderate upper-respiratory tract illness, croup, tonsilitis
Seasonal influenza	Sialic acids	Fever, rhinorrhea or stuffy nose, coryza, sore throat, cough, headache, myalgia	Mild to moderate upper-respiratory tract illness, bronchitis, croup
RSV	Nucleolin	Fever, rhinorrhea, coryza, sore throat, cough, wheezing, shortness of breath	Mild to moderate upper-respiratory tract illness, bronchitis, bronchiolitis, croup
Enterovirus D68	Sialic acids alpha2-6	Rhinorrhea, sneezing, cough, mouth blisters, myalgia; wheezing and dyspnea in more severe cases	Mild to moderate upper-respiratory tract illness, bronchitis, bronchiolitis, pneumonia
Pandemic influenza	Sialic acids	Fever, coryza, rhinorrhea or stuffy nose, sore throat, cough, headache, shortness of breath, dyspnea, myalgia	Bronchitis, croup, pneumonia, diffuse alveolar damage, acute respiratory distress syndrome, respiratory failure
SARS-CoV	ACE2	Fever, chills, cough, shortness of breath, dyspnea, myalgia	Rapidly progressive pneumonia, diffuse alveolar damage, severe acute respiratory distress syndrome, respiratory failure, fibrosis
MERS-CoV	CD26	Fever, chills or rigors, coryza, sore throat, non-productive cough, sputum production, shortness of breath, dyspnea, headache, vomiting, diarrhea, myalgia	Rapidly progressive pneumonia, diffuse alveolar damage, severe acute respiratory distress syndrome, respiratory failure, septic shock and multi-organ failure



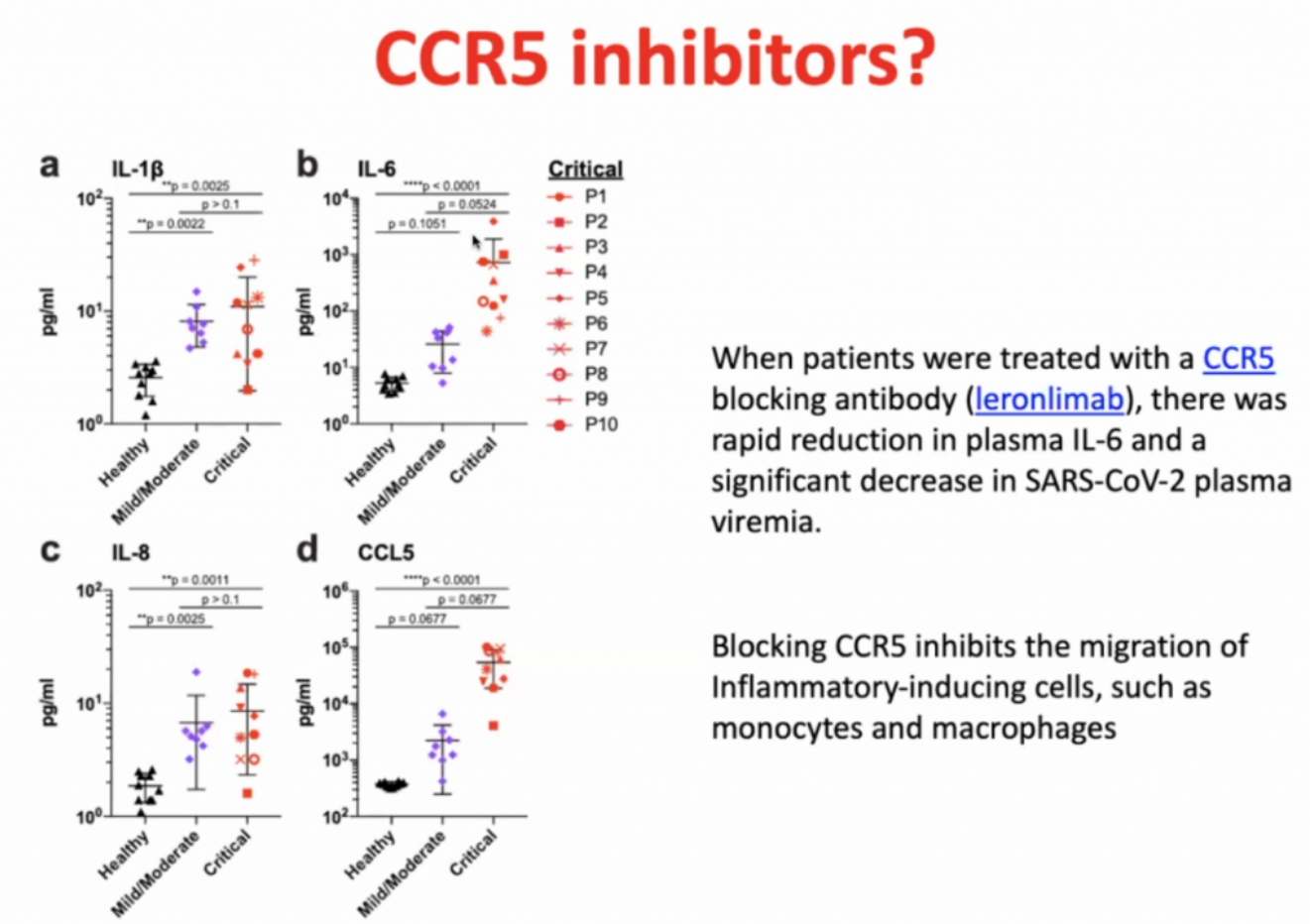
Dose of the virus (viral load) is key to how you respond to the virus – Initial High dose in viral load likely will lead to high inflammatory response; Low dose (non-robust virus replication) may cause a less severe inflammatory response.





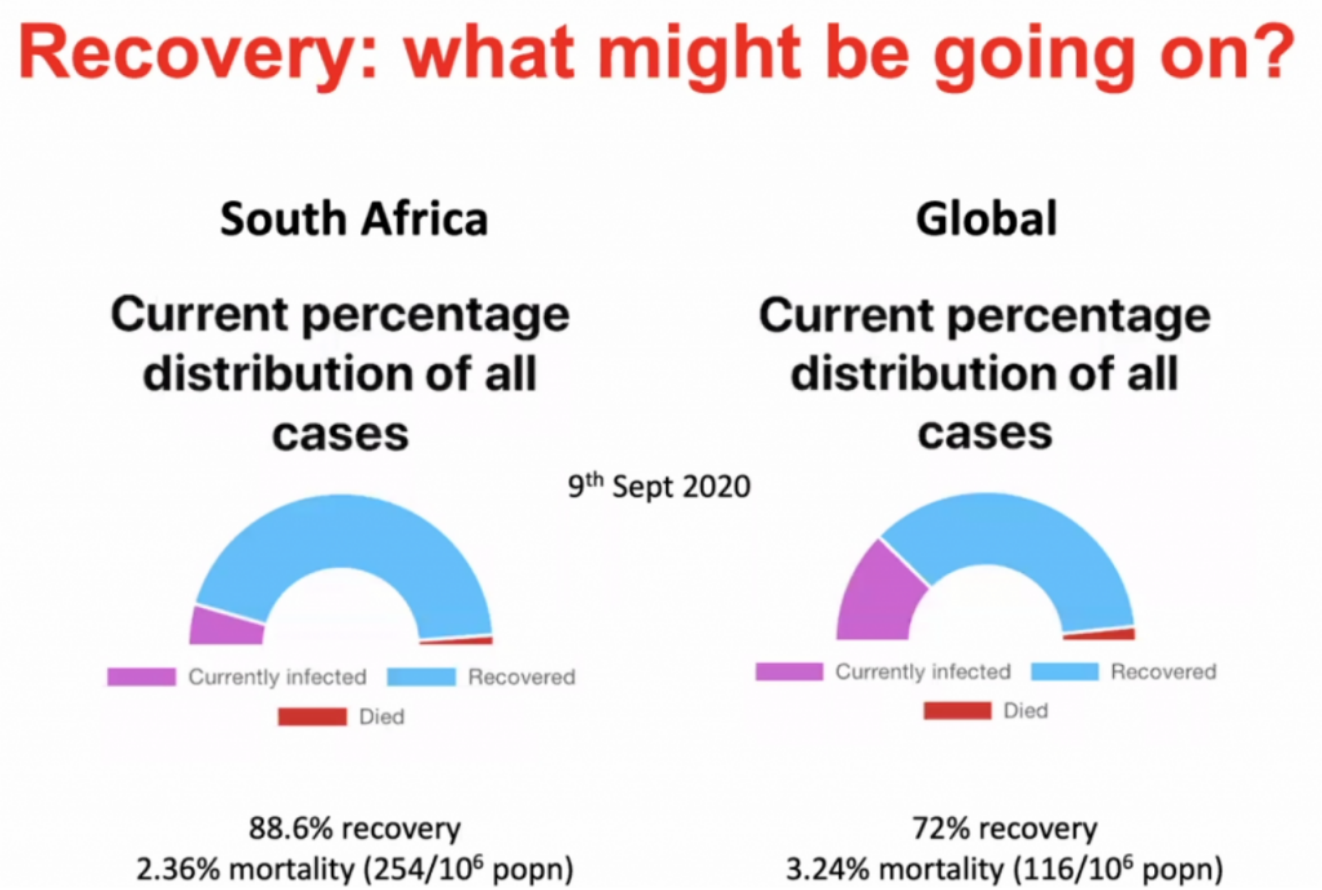
CCL's allow leucocytes to migrate, hence in a **cytokine storm**, with high level of **migration**, the leucocytes causes severe local inflammation due to migration of leucocytes to local

sites.



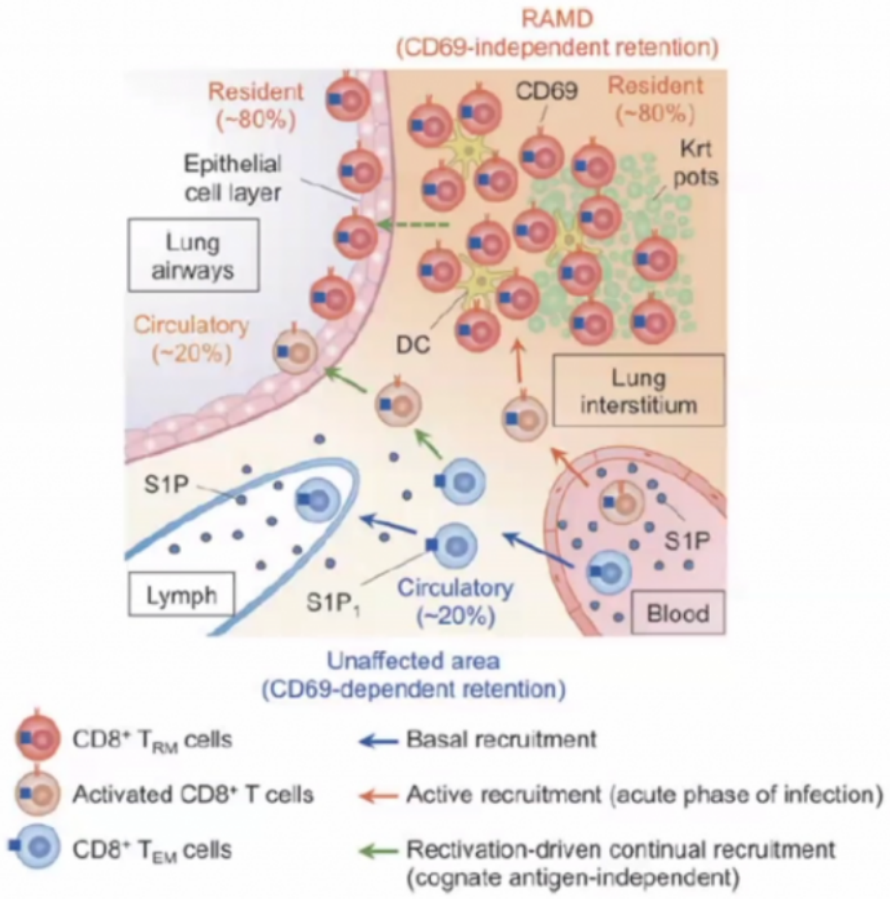
CCL5 blocking antibodies leads to rapid reduction of IL-6. Dexamethasone is not so much an inhibitor of CCR5, but it prevents the hyperinflammation by inhibiting the majority of the inflammatory pathway.

Recovery: what might be going on?



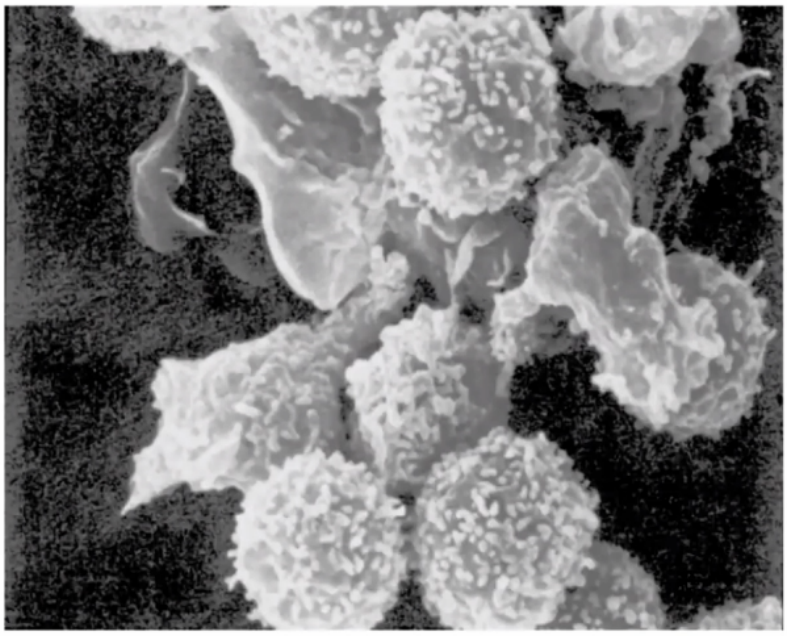
CD8 cells

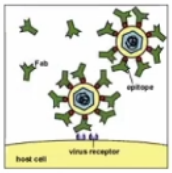
Special CD8+ cells in the lung: possible protection



Within interstisium, the CD8 cells are present and

$CD4^+$ cells help B cells makes antibody and CD8 cells kill target cells



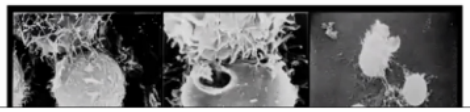


Antibodies

B cells

Expansion of CD4 cells

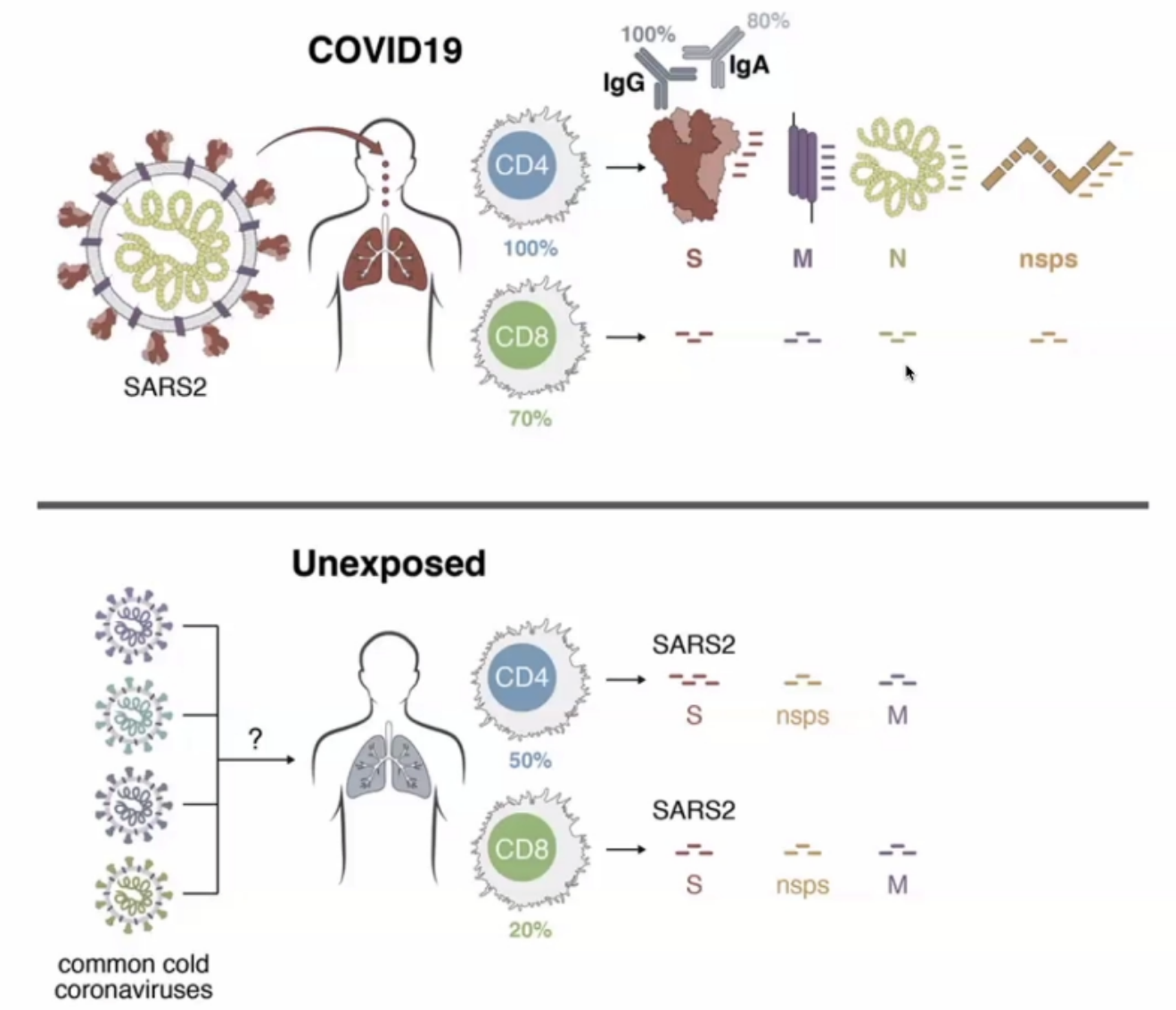
CD8 cytotoxic T lymphocytes



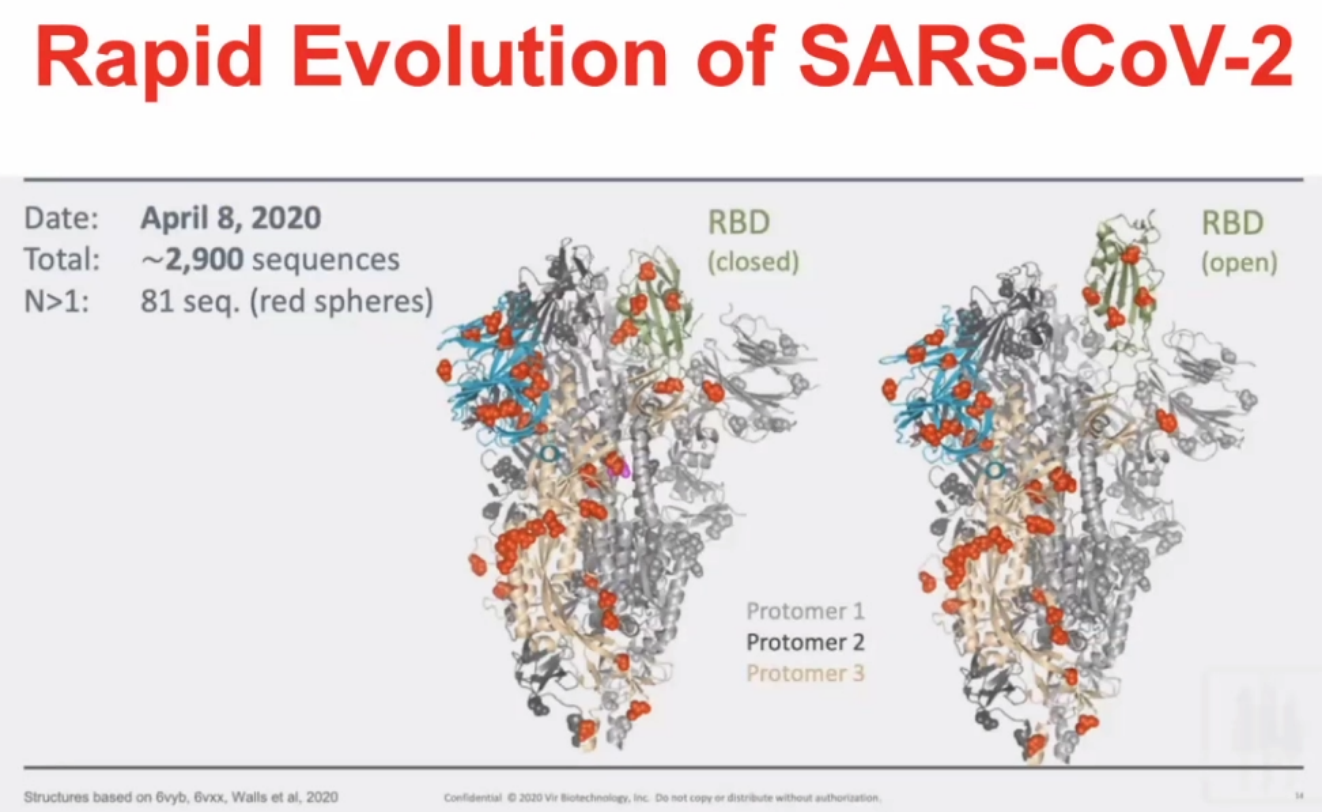
CD4 cells activates CD8 cells, hence called T-helper cells.

Is there Evidence for pre-existing immunity?

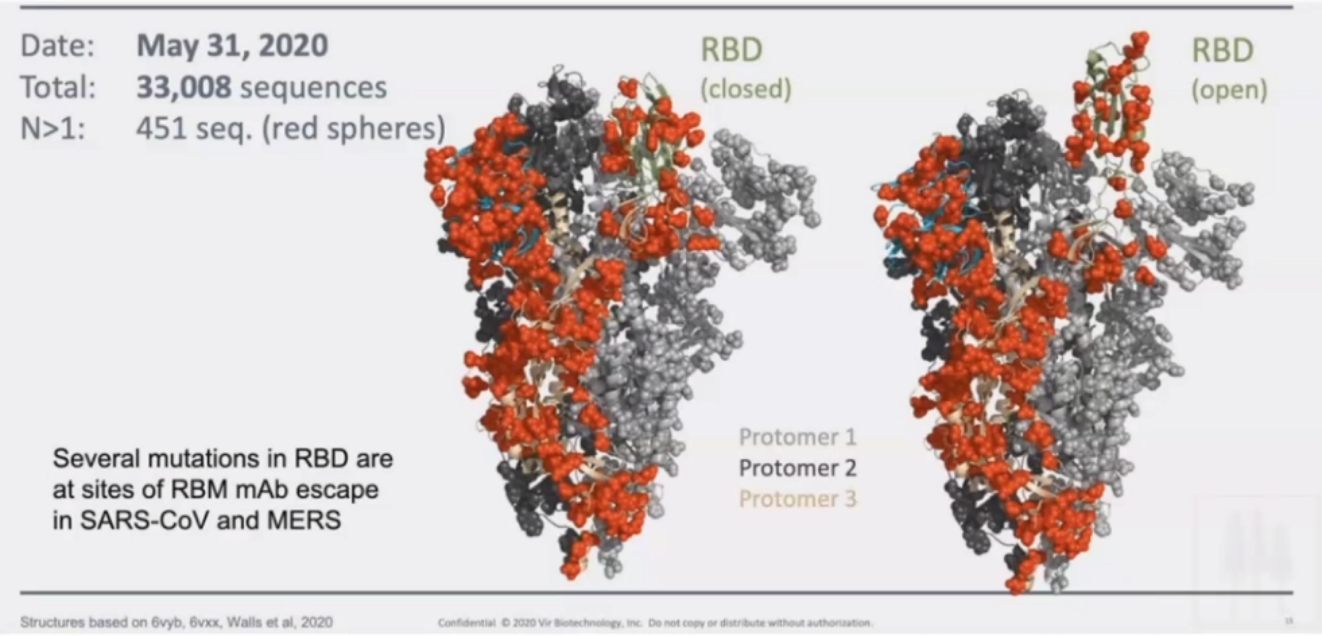
- Preexisting T cell immunity existed to H1N1 in the adult population (Greenbaum et al 2009)
- The presence of cross-reactive T cells was found to correlate with less severe disease (Sridhar et al 2013; Wilkinson et al 2012)
- Substantial cross-reactive coronavirus T cell memory has been observed (Grifoni et al 2020)



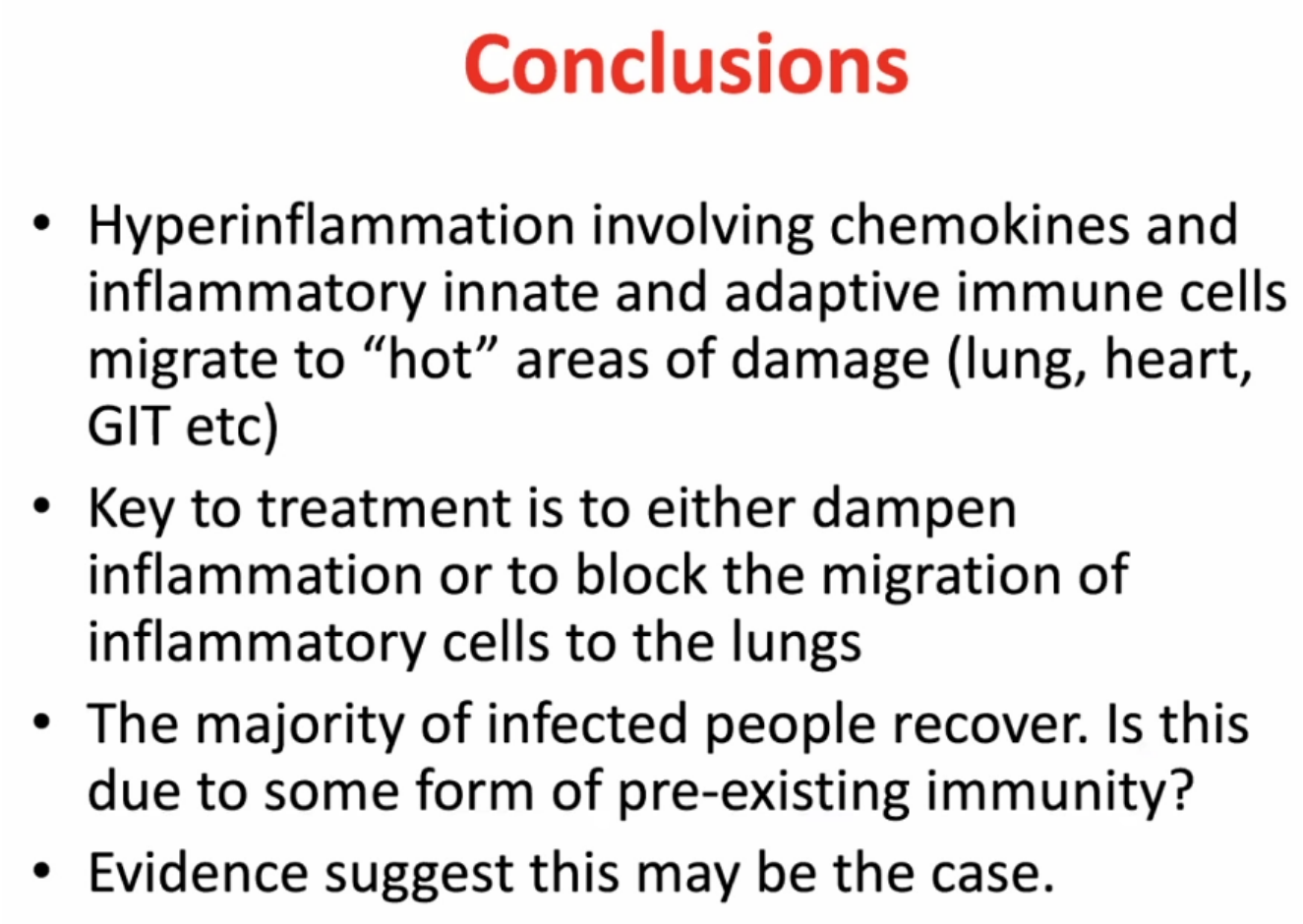
T-cell responses are very prevalent to COVID-19 exposed individuals. BUT CD4 cells and CD8 cells can also react to the SARS2 viral proteins in unexposed individuals.



RBD – receptor binding domain (Spike-protein); Orange is the amount of amino acids which are changeable.



Orange amino acids are those which are changeable – illustrating how the virus has mutated in a month.



Section 7.1 – Publications by Candidate

COVID-19 Related Laboratory Analyte Changes and the Relationship between SARS-CoV-2 and HIV, TB and HbA1c in South Africa

Reinhardt Hesse, Dieter van der Westhuizen, Jaya George

We conducted a retrospective analysis on data of all adults tested for SARS-CoV-2 across our laboratory network in South Africa over a 4-month period. Out of 842,197 tests 11.7% were positive and 88.3% negative. The prevalence of HIV was 6.25 and 6.31% in the SARS-CoV-2 positive and negative cohort

respectively (p=0.444). However, the prevalence of HIV positive individuals in the critical cohort (9.15%) was higher than in the non-critical group (6.24%) (p=0.011). Active tuberculosis infection was approximately 50% less in SARS-CoV-2 positive than in negative individuals. The prevalence of uncontrolled diabetes was 3.4 times higher in SARS-CoV-2 positive cases, but was not higher in the critical vs. non-critical cases (p=0.612). The neutrophil-to-lymphocyte-ratio, coagulation markers, urea, cardiac, and liver related analytes were significantly elevated in the critical compared to non-critical cases. Platelet count and creatinine concentration did not differ significantly between the two groups. These findings do not support increased prevalence of HIV or tuberculosis in individuals with SARS-CoV-2 infection but do suggest an association of increased disease severity with HIV positive status. Uncontrolled diabetes was positively associated with a significantly higher prevalence of SARS-CoV-2 and our investigation into analyte changes associated with SARS-CoV-2 disease severity supported previous findings of raised inflammatory markers, coagulation markers, liver and cardiac related analytes and urea, but not for creatinine and platelet count.

See the full article (book chapter) below:

https://www.researchgate.net/publication/343650512_COVID-19_Related_Laboratory_Analyte_Changes_and_the_Relationship_between_SARS-CoV-2_and_HIV_TB_and_HbA1c_in_South_Africa

> *Acute Kidney Injury during the COVID-19 Pandemic – Experience from Two Tertiary Centres in South Africa*
>
> *Nina E. Diana, Ismail S. Kalla, Nicola Wearne, Sarah Kariv, Bianca Davidson, Jody Rusch, Zibya Barday, Abid M. Sheikh, Samantha Reiche, Farzahna Mohamed, Sara Saffer, Chandni Dayal, Jacqueline P. Venturas, Jarrod M. Zamparini, Dieter van der Westhuizen, Sean Wasserman, Nectarios Papavarnavas, Linda Boloko, Timothy de Wet, Graham Paget, Adam Mahomed,*

Sagren Naidoo and Erika S.W. Jones

Background: The first case of SARS-CoV-2 in South Africa [SA] was documented in March 2020. By October, the total cases for the Western Cape and Gauteng Provinces were 331,425 with 8456 fatalities. The aim of this study was to describe the prevalence of acute kidney injury [AKI] in hospitalized patients with COVID-19 in two tertiary centres in SA. Methods: SARS-CoV-2 positive patients admitted to two tertiary centres in SA between 18 March and 31 August 2020 were included in the study. Demographic data, pre-existing comorbidities, admission variables, laboratory data, management and hospital outcomes were captured. Exclusion criteria included age <18 years, pre-existing Stage 4 or 5 chronic kidney disease and prior renal transplant. Outcomes assessed were the need for acute dialysis, recovery from AKI, discharge and death. Results: AKI occurred in 374/1102 (33.9%) patients admitted to the two hospitals. Within the AKI cohort, 91 (24.3%) patients required intensive care unit [ICU] management, and 32 (8.6%) received kidney replacement therapy. Older age (P = 0.001), pre-existing hypertension [HPT] (P = <0.0001) and biochemical evidence of severe disease, including high ferritin, lactate dehydrogenase, d-dimer and C-reactive protein, were significantly higher in the patients with AKI versus those without. AKI Stage 3 had a higher mortality and lower rates of renal recovery upon discharge. AKI was significantly associated with an increased utilization of ICU resources, prolonged length of stay and mortality. Conclusion: This study reports the largest cohort of COVID-19-associated AKI in Africa. Older age, HPT and severe COVID-19 infection were significantly higher in patients with COVID-19 who developed AKI. This cohort had high rates of AKI which was associated with adverse outcomes, including mortality.

See full article below:

https://www.researchgate.net/publication/345977288_Acute_Kidne

y_Injury_during_the_COVID-19_Pandemic_-_Experience_from_Two_Tertiary_Centres_in_South_Africa

or download a pdf copy:

AcuteKidneyInjuryduringtheCOVID-19PandemicExperiencefromTwoTertiaryCentresinSouthAfricaDownload